

Herbs for health, but how safe are they?



Courtesy, Research Centre for Ethnomedicines, Tojama Medical and Pharmaceutical University, Japan.

Japanese gentian (*Gentiana scabra* Bunge var. *buergeri* Maxim), whose roots and underground stems are used as an appetite stimulant, and to treat herpes zoster and inflammatory conditions of internal organs.

Herbal medicines are popular. They are extensively used in the developing world, where in many places they offer a more widely available and more affordable alternative to pharmaceutical drugs. In Africa, for example, up to 80% of the population depends on them, according to WHO estimates. A recent study by the Roll Back Malaria Initiative found that in Ghana, Mali, Nigeria and Zambia, herbal medicine is the first choice for home treatment of nearly two thirds of children with high fever. In India, where the traditional Ayurvedic medicine employs over 1200 different herbs, herbal medicine is regularly used by about 65% of the population.

Herbal medicines are also popular in developed countries — the same WHO estimates state that 50% of Canadians and 75% of people in France have tried complementary or alternative medicine, which often includes herbal remedies. And in Japan, 85% of doctors prescribe not only modern medicine but also the traditional herbal medicine (called *Kampo*), which is covered by health insurance.

Herbal medicines are also profitable. Worldwide, they represent a market value of about US\$ 43 billion a year, according to WHO. In the US, alone, over 1500 herbal medicines are sold annually for a total of nearly US\$ 5 billion and now constitute the fastest

growing sector of the US pharmaceutical market, according to the US president's commission on dietary supplements.

The growing popularity of these remedies is fuelling — and is to some extent fuelled — by increasing scientific interest in herbal medicine. WHO estimates that of the 35 000–70 000 species of plants that are used for medicinal purposes around the world, some 5000 have been submitted to biomedical scrutiny. Scientific evidence of efficacy is beginning to emerge from randomized controlled trials in which herbs compare favourably with placebo. Examples include St John's wort for mild depression, ginkgo biloba for some forms of dementia, saw palmetto for benign prostatic hyperplasia, and horse chestnut seeds for chronic venous insufficiency, to mention only four. And, of course, a number of commonly used pharmaceutical products are of botanical origin — aspirin, digitoxin, and quinine are three well-known examples.

Another reason for the growing popularity of herbal medicines is that many people believe they are safer, “more natural,” than pharmaceuticals. But as Dr Saul Green, a biochemist and board member of the nonprofit US National Council Against Health Fraud, notes: “Natural doesn't mean safe. You can find a dozen or more poisons that are totally natural.”

Herbal medicines, however natural, can cause serious illnesses, from allergy to liver or kidney malfunction, to cancer, and even death. In terms of carcinogenicity, for example, the toxicological potential of natural plant chemicals is roughly the same as that of synthetic chemicals, according to US toxicologist Dr Lois Gold, head of the carcinogenic potency project at the University of California at Berkeley. And the fact that herbal products tend to be taken for long periods at doses close to their toxic range doesn't help, she notes.

Blindness, too, has been attributed to the use of herbal medicines. A study published in the *Journal of Tropical Medicine and Hygiene* in 1994 reported that 25% of corneal ulcers in the United Republic of Tanzania were linked to the use of traditional eye medicines, of which many are based on herb extracts. Another study, published in the *British Journal of Ophthalmology* in 1976, found that they were associated with 26% of childhood blindness cases in Malawi. A lack of proper sterilization, along with inclusion of urine, saliva, or breast milk in some of

these medicines, gives pathogens ample opportunity to thrive in eyes already hard hit by injury or infection.

Perhaps the biggest problems with herbal medicines are a lack of standardization and of safety regulations. Standardization of a herbal medicine that may contain hundreds of chemical constituents, with little or no evidence indicating which might be responsible for the presumed or proven therapeutic effect, is a particularly thorny issue.

Food or medicine

Moreover, rules and regulations concerning herbal medicines vary greatly from country to country. "Some countries regulate them as food, others as medicines," says Dr Alan Randell of the FAO/WHO Food Standards Programme in Rome. For the most part herbal medicines aren't tightly regulated. "This is an industry that's out of control and has been for a very long time. By and large, the people running the industry want it to stay that way," says Randell. In 1997, the Codex Alimentarius Commission, an international body that regulates food standards, considered issuing rules for potentially harmful herbs and dietary supplements. But, according to Randell, the health food industry pressured the Codex against regulating herbs, and the Codex ultimately decided that herbal medicines didn't fall under the category of food and thus weren't subject to its regulations.

Worldwide, only 64 of WHO's 191 member states regulate herbal medicines. Dr Xiaorui Zhang, head of WHO's traditional medicine unit, agrees that the regulation and standardization of herbal medicines "clearly represent important problems" but she points out that considerable effort is being put into tackling the problems. In 1998, for example, WHO published a review of regulatory information from 50 countries.

Last year, Zhang's unit published guidelines on methods of evaluating traditional medicine therapies, including herbal medicines.

Over the past decade WHO's work on herbal medicines has included the preparation of a series of monographs on medicinal plants, based on input from an international panel of 170 experts. About 100 monographs are planned, of which 28 appeared in 1999 in a first volume, a further 30 are in press in a second volume and work is well advanced on the remaining 40 or so, which will appear in a third volume. For each plant, the monographs give a definition, synonyms (including vernacular names), a description, identification of material of medicinal interest in the plant, and a wealth of scientific information about purity, chemical tests, pharmacology, warnings, precautions, ad-

verse reactions, dosage, plus a copious scientific reference list. Zhang's unit has also started a project to run clinical trials — being conducted in collaboration with the Roll Back Malaria initiative — of medicinal herbs. Trials of three herbs with antimalarial potential are under way in Africa.

In Europe, the European Medicines Evaluation Agency (EMEA) set up a herbal medicinal products working party in May 1997 that, among other things, prepares guidelines for manufacturers seeking marketing authorization for their products. In the UK, the Medicines Control Agency (MCA) has launched an ethnic medicines forum to improve safety and quality standards of "unlicensed ethnic medicines". And Germany boasts a widely acclaimed regulatory body, its "Commission E", that was set up in 1978 to assess the safety and efficacy of herbal medicines and has done so for about 400 of them, although, some critics complain, with insufficient information about scientific sources.

FDA reports

In the US, a 1994 law reportedly pushed through by herbal industry representatives prevents government officials from tightly regulating herbal supplements. The only safety measure in place is a system whereby consumers and health professionals can voluntarily report herb-related adverse events to the Food and Drug Administration. The FDA makes these reports available publicly, and on a few occasions has issued recalls of products deemed especially dangerous. For instance, in February of 2000, the FDA recalled five Chinese herbal products after discovering that they contained potentially dangerous levels of two prescription diabetes drugs, glyburide and phenformin. And in August 2000, in a move to encourage better manufacturing practices in industry, the FDA issued a "guidance for industry" document that sets out the criteria it urges manufacturers to comply with when they wish to market a botanical drug product — "including those botanical products currently lawfully marketed as foods and dietary supplements".

The US Pharmacopoeia, a non-governmental organization that establishes medicine quality standards recognized around the world, is launching a new programme to assess the quality of dietary supplements, including herbals. And the government sponsored National Toxicology Program is currently assessing about a dozen herbal medicines for safety, including goldenseal, comfrey, pulegone, ginkgo, Echinacea, aloe, ginseng, kava kava, milk thistle, and Thujone.

Clearly, without strict safety regulations, dangerous herbal preparations are reaching

consumers. In Belgium, 70 people who took a regimen of Chinese dietary herbs developed renal problems serious enough to require dialysis or a kidney transplant. A research team led by Dr Joelle Nortier at the Université Libre de Bruxelles discovered that among the herbs consumed by these people was *Aristolochia fangchi*, which contains high concentrations of the potent carcinogen and kidney toxin aristolochic acid, and which was mistakenly included in the regimen by the manufacturer.

Contamination problems

Pesticide residues present in or on herbs are another problem. In a study published this year in the *Bulletin of Environmental Contamination and Toxicology*, researchers at the Suez Canal University in Ismailia, Egypt, examined five spices — caraway, ginger, cumin seeds, cinnamon, and anise — they had purchased at a local market in Egypt. To their dismay, they discovered that the cumin seeds showed high levels of the organophosphate pesticide profenofos — 0.37g/kg, or nearly twice the residue the WHO and Codex Alimentarius Commission permit in vegetables. This pesticide is known to cause headaches, nausea, dizziness, intestinal cramps, and diarrhoea in high doses. The finding is especially troubling because Egyptian parents commonly give their children cumin to relieve coughs, aches, or itching, and children's low body weights make them especially vulnerable to the pesticides' effects.

In the US, Dr Richard Ko, a food and drug scientist at the California State Department of Health Services in Sacramento, says that of 260 Asian herbal products his department has tested, about one in three were found to contain heavy metals or undeclared ingredients, including prescription drugs. A US company, ConsumerLab.com, has tested hundreds of herbal products and posted the results on its website. "We've found ginseng products contaminated with pesticides and St John's wort with small levels of cadmium," says Dr Tod Cooperman, the company's president. "In our latest tests, we found one Echinacea product that had three times the WHO accepted level of microbial contamination."

All in all, herbal medicines inhabit a largely uncharted territory. Even the jungle of names for the different herbs is a regulator's nightmare. Is *Eupatorium perfoliatum* "feverwort", "thoroughwort", or "boneset"? Take your pick. The same for *Serenoa repens* or *Sabal serrulata* or *Corypha repens* or *Brabea serrulata*. Clearly, though, when it comes to safety, what's in a name is not what counts, but what's in the herb itself. And that's another nightmare. ■

Christie Aschwandten,
Nederland, Colorado, USA